



EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to a combination of *Lactobacillus paracasei* CNCM I-1688 and *Lactobacillus salivarius* CNCM I-1794 and reduction of gastrointestinal discomfort (ID 2972), decreasing potentially pathogenic gastrointestinal microorganisms (ID 2972), improved lactose digestion (ID 2972) and increasing IL-10 production (ID 2973) (further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006

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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to a combination of *Lactobacillus paracasei* CNCM I-1688 and *Lactobacillus salivarius* CNCM I-1794 and reduction of gastro-intestinal discomfort (ID 2972), decreasing potentially pathogenic gastro-intestinal microorganisms (ID 2972), improved lactose digestion (ID 2972) and increasing IL-10 production (ID 2973) (further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2,3}

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ABSTRACT

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to provide a scientific opinion on health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 in the framework of further assessment related to a combination of *Lactobacillus paracasei* CNCM I-1688 and *Lactobacillus salivarius* CNCM I-1794 and reduction of gastro-intestinal discomfort, decreasing potentially pathogenic gastro-intestinal microorganisms, improved lactose digestion and increasing IL-10 production. The food constituent that is the subject of the health claims, a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794, is sufficiently characterised. The evidence provided did not establish that the proposed claimed effect, increasing IL-10 production, is a beneficial physiological effect. On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and a beneficial physiological effect related to an increase in IL-10 production. The claimed effect, reduction of gastro-intestinal discomfort, is a beneficial physiological effect for the general population. The claimed effect, decreasing potentially pathogenic gastro-intestinal microorganisms, might be a beneficial physiological effect for the general population. The claimed effect, improved lactose digestion, is a beneficial physiological effect for individuals with lactose maldigestion. No human intervention studies were provided from which conclusions could be drawn for the scientific substantiation of the above-mentioned claims. On the basis of the data provided, the Panel concludes that a cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and reduction of gastro-intestinal discomfort, decreasing potentially pathogenic gastro-intestinal microorganisms and improved lactose digestion. © European Food Safety Authority, 2012

¹ On request from the European Commission, Question No EFSA-Q-2012-00200, EFSA-Q-2012-00201, adopted on 28 June 2012.

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KEY WORDS

Lactobacillus paracasei CNCM I-1688, *Lactobacillus salivarius* CNCM I-1794, gastro-intestinal discomfort, pathogens, lactose digestion, IL-10, health claims.

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. The Commission has agreed with EU Member States that a certain number of Article 13 health claims would be eligible for further assessment by EFSA in order to be able to take a final decision on whether or not to include these claims in the list of permitted health claims. This opinion addresses the scientific substantiation of health claims in relation to a combination of *Lactobacillus paracasei* CNCM I-1688 and *Lactobacillus salivarius* CNCM I-1794 and reduction of gastro-intestinal discomfort, decreasing potentially pathogenic gastro-intestinal microorganisms, improved lactose digestion and increasing IL-10 production. The scientific substantiation is based on the information provided by the competent Authority of Italy for further assessment of this claim.

The food constituent that is the subject of the health claims is a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794. The Panel considers that the combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 is sufficiently characterised.

Reduction of gastro-intestinal discomfort

The claimed effect which is proposed for further assessment relates to reduction of gastro-intestinal discomfort. The proposed target population is the general population. Reduction of gastro-intestinal discomfort is a beneficial physiological effect.

No human intervention studies were provided from which conclusions could be drawn for the scientific substantiation of the claim.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and reduction of gastro-intestinal discomfort.

Decreasing potentially pathogenic gastro-intestinal microorganisms

The claimed effect which is proposed for further assessment relates to a decrease in potentially pathogenic gastro-intestinal microorganisms. The proposed target population is the general population. Decreasing potentially pathogenic gastro-intestinal microorganisms might be a beneficial physiological effect.

No human intervention studies were provided from which conclusions could be drawn for the scientific substantiation of the claim.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and decreasing potentially pathogenic gastro-intestinal microorganisms.

Improved lactose digestion

The claimed effect which is proposed for further assessment relates to improved lactose digestion. Improved lactose digestion is a beneficial physiological effect for individuals with lactose maldigestion.

No human intervention studies were provided from which conclusions could be drawn for the scientific substantiation of the claim.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and improved lactose digestion.

Increasing IL-10 production

The claimed effect which is proposed for further assessment relates to increasing IL-10 production. The proposed target population is the general population. The Panel notes that increasing IL-10 production by peripheral blood mononuclear cells is not a beneficial physiological effect *per se*, but needs to be linked to a beneficial physiological or clinical outcome.

The Panel considers that the evidence provided did not establish that increasing IL-10 production is a beneficial physiological effect.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and a beneficial physiological effect related to an increase in IL-10 production.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

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TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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EFSA DISCLAIMER

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INTRODUCTION

The Commission has agreed with EU Member States that a certain number of Article 13 health claims would be eligible for further assessment by EFSA in order to be able to take a final decision on whether or not to include these claims in the list of permitted health claims. These claims include already assessed claims related to micro-organisms which the Panel considered to be not sufficiently characterised and claims for which the NDA Panel concluded that there was insufficient evidence to establish a cause and effect relationship between the consumption of the food and the claimed effect.

Following an opinion of the NDA Panel pursuant to Article 13 of Regulation (EC) No 1924/2006⁴ in which the Panel concluded that the data available were not sufficient to characterise a combination of *Lactobacillus paracasei* I-1688 and *Lactobacillus salivarius* I-1794 (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2009), EFSA received additional information from the competent Authority of Italy for further assessment of this claim. The information provided in the framework of further assessment for the health claims which are the subject of this opinion is tabulated in Appendix C.

ASSESSMENT

1. Characterisation of the food/constituent

The food constituent that is the subject of the health claim is a combination of *Lactobacillus paracasei* CNCM I-1688 and *Lactobacillus salivarius* CNCM I-1794.

For *L. paracasei* CNCM I-1688, a culture collection number from the French National Collection of Cultures of Microorganisms (CNCM) (I-1688) was provided. The CNCM is a restricted-access non-public collection which has the status of an International Depositary Authority under the Budapest Treaty. Data on the identification and characterisation of *L. paracasei* CNCM I-1688 at species and strain level, by using both phenotypic (carbohydrate fermentation profiles) and genotypic (16S rRNA gene sequence analysis, plasmidic profile, ARDRA, RAPD, Rep-PCR, PFGE) methods, were provided in the applications for further assessment and in the accompanying references (AAT, 2011a, unpublished; Bonetti et al., 2002; Morelli, 1996, unpublished; Morelli, 1997, unpublished; Pedraglio, 2004). The Panel considers that *L. paracasei* CNCM I-1688 is sufficiently characterised.

For *L. salivarius* CNCM I-1794, a culture collection number from the CNCM, I-1794, was provided. Data on the identification and characterisation of *L. salivarius* CNCM I-1794 at species and strain level, by using both phenotypic (carbohydrate fermentation profiles) and genotypic (16S rRNA gene sequence analysis, plasmidic profile, ARDRA, RAPD, Rep-PCR, PFGE) methods, were provided in the applications for further assessment and in the accompanying references (AAT, 2011b, unpublished; Bonetti et al., 2002; Morelli, 1996, unpublished; Morelli, 1997, unpublished; Pedraglio, 2004). The Panel considers that *L. salivarius* CNCM I-1794 is sufficiently characterised.

The Panel considers that the food constituent, the combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794, is sufficiently characterised.

2. Relevance of the claimed effect to human health

2.1. Reduction of gastro-intestinal discomfort (ID 2972)

The claimed effect which is proposed for further assessment is: “Is a probiotic; Contributes to a healthy digestive system by supporting the gut flora through an increased number of positive lactobacillus in the intestine; useful to maintain a healthy intestinal flora by adhering to the mucosa; Improves intestinal barrier function by competing (steric encumbrance) against pathogens; Reduces

⁴ Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

gastro-intestinal discomfort; Necessary to maintain a healthy digestive system by production of specific enzymes (eg: beta-galactosidase)". The proposed target population is the general population.

The Panel considers that reduction of gastro-intestinal discomfort is a beneficial physiological effect.

2.2. Decreasing potentially pathogenic gastro-intestinal microorganisms (ID 2972)

The claimed effect which is proposed for further assessment is: "Is a probiotic; Contributes to a healthy digestive system by supporting the gut flora through an increased number of positive lactobacillus in the intestine; useful to maintain a healthy intestinal flora by adhering to the mucosa; Improves intestinal barrier function by competing (steric encumbrance) against pathogens; Reduces gastro-intestinal discomfort; Necessary to maintain a healthy digestive system by production of specific enzymes (eg: beta-galactosidase)". The proposed target population is the general population.

The Panel notes that it is not possible to define the exact number of the different microbial groups which constitute a normal/healthy microbiota. Increasing the number of any groups of microorganisms, including lactobacilli, is not in itself considered to be a beneficial physiological effect.

The Panel assumes that the claimed effect refers to decreasing potentially pathogenic gastro-intestinal microorganisms. The Panel considers that decreasing potentially pathogenic gastro-intestinal microorganisms might be a beneficial physiological effect.

2.3. Improved lactose digestion (ID 2972)

The claimed effect which is proposed for further assessment is: "Is a probiotic; Contributes to a healthy digestive system by supporting the gut flora through an increased number of positive lactobacillus in the intestine; useful to maintain a healthy intestinal flora by adhering to the mucosa; Improves intestinal barrier function by competing (steric encumbrance) against pathogens; Reduces gastro-intestinal discomfort; Necessary to maintain a healthy digestive system by production of specific enzymes (eg: beta-galactosidase)". The proposed target population is the general population.

The Panel assumes that the claimed effect refers to improved lactose digestion, and that the target population is individuals with lactose maldigestion. Lactose maldigestion is a common condition caused by reduced levels of intestinal lactase.

The Panel considers that improved lactose digestion is a beneficial physiological effect for individuals with lactose maldigestion

2.4. Increasing IL-10 production (ID 2973)

The claimed effect which is proposed for further assessment is: "Supports your natural (immune) defence system by increasing the IL-10 production in peripheral blood mononuclear cells (PBMC); Necessary to maintain the natural defences/helps to maintain a balanced immune system (increasing the IL-10 production)". The proposed target population is the general population.

The Panel notes that the claimed effect "supports your natural (immune) defence system /necessary to maintain the natural defences/helps to maintain a balanced immune system" is not sufficiently defined, and assumes that the claimed effect relates to increasing IL-10 production by peripheral blood mononuclear cells. The Panel notes that increasing IL-10 production by peripheral blood mononuclear cells is not a beneficial physiological effect *per se*, but needs to be linked to a beneficial physiological or clinical outcome.

The references provided in relation to the claim were related to the methodology for bacterial strain identification, *in vitro* studies on the immunomodulatory properties of the combination of the strains (i.e. phenotype of the lymphocytic subpopulations, and cytokine production such as IL-10, IL-12, INF γ ; (Castellazzi et al., 2007; Castellazzi, 2007a, unpublished)), and a patent (Dondi and Malfa,

2007) which reported on the use of the lactic bacteria that are the subject of the claim for the preparation of a composition suitable for modulating the immune system, and also on the *in vitro* effects of the strains on lymphocytes (lymphocyte proliferation, phenotype of the lymphocytic subpopulations, and cytokine production), but without providing primary data. Two references reported on the same human intervention study (Castellazzi, 2007a, unpublished; Valsecchi et al., 2008), which was an open-label, single arm (non-placebo controlled) study which investigated the effects of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 on symptoms of allergy (atopic dermatitis, rhino-conjunctivitis, urticaria, contact dermatitis, oral allergy syndrome and food allergies), and on immunological parameters (e.g. lymphocyte population, natural killer cell activity and cytokine production), in 20 children with atopic disorders. The Panel notes that this study was a single-arm study with no control group, and considers that no conclusions can be drawn from this study for the scientific substantiation of the claim.

The Panel considers that the evidence provided does not establish that increasing IL-10 production by peripheral blood mononuclear cells is a beneficial physiological effect.

The Panel concludes that a cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and a beneficial physiological effect related to an increase in IL-10 production.

3. Scientific substantiation of the claimed effect

3.1. Reduction of gastro-intestinal discomfort (ID 2972)

The references provided in relation to this claim were related to methodologies for bacterial strain identification (Jensen et al., 1993; Ventura et al., 2000); patents for the use of two *Lactobacillus* strains (*L. gasseri* P-17632 and/or *L. salivarius* CNCM I-1794) other than the combination that is the subject of the claim against *Candida albicans* (Dondi, 2004, 2007); a patent on a method for the selection of *Lactobacillus* strains, including *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794, indicated to be useful for the treatment of various disorders of the gastro-intestinal tract because of their capability to produce lactic acid (Pedraglio, 2004); and a human intervention study on the viability of the combination of the strains that is the subject of the claim through the human intestinal tract (Bonetti et al., 2002). The Panel notes that these studies did not address outcome measures related to the claimed effect, and considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

The Panel notes that no human studies were provided from which conclusions could be drawn for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of the combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and reduction of gastro-intestinal discomfort.

3.2. Decreasing potentially pathogenic gastro-intestinal microorganisms (ID 2972)

The references provided in relation to this claim were related to methodologies for bacterial strain identification (Jensen et al., 1993; Ventura et al., 2000); a patent on a method for the selection of *Lactobacillus* strains, including *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794, indicated to be useful for the treatment of various disorders of the gastro-intestinal tract because of their capability to produce lactic acid (Pedraglio, 2004); and a human intervention study on the viability of the combination of the strains that is the subject of the claim through the human intestinal tract (Bonetti et al., 2002). The Panel notes that these studies did not address outcome measures related to the claimed effect, and considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

Two patents for the use of *L. gasseri* P-17632 and/or *L. salivarius* CNCM I-1794 against *Candida albicans* (Dondi, 2004, 2007) were also provided. The Panel notes that only one of the strains mentioned in the patents is part of the combination of strains that is the subject of the claim, and that no primary data were provided that could be used for the substantiation of the claim. The Panel considers that no conclusions can be drawn from these patents for the scientific substantiation of the claim.

The Panel notes that no human studies were provided from which conclusions could be drawn for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of the combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and decreasing potentially pathogenic gastro-intestinal microorganisms.

3.3. Improved lactose digestion (ID 2972)

The references provided in relation to this claim were related to methodologies for bacterial strain identification (Jensen et al., 1993; Ventura et al., 2000); patents for the use against *Candida albicans* of two *Lactobacillus* strains (*Lactobacillus gasseri* P-17632 and/or *L. salivarius* CNCM I-1794) other than the combination that is the subject of the claim (Dondi, 2004, 2007); a patent on a method for the selection of *Lactobacillus* strains, including *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794, indicated to be useful for the treatment of various disorders of the gastro-intestinal tract because of their capability to produce lactic acid (Pedraglio, 2004); and a human intervention study on the viability of the combination of the strains that is the subject of the claim through the human intestinal tract (Bonetti et al., 2002). The Panel notes that these studies did not address outcome measures related to the claimed effect, and considers that no conclusions can be drawn from these references for the scientific substantiation of the claim.

The Panel notes that no human studies were provided from which conclusions could be drawn for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and improved lactose digestion.

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food constituent, a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794, which is the subject of the health claims, is sufficiently characterised.

Reduction of gastro-intestinal discomfort (ID 2972)

- The claimed effect proposed for further assessment relates to reduction of gastro-intestinal discomfort. The proposed target population is the general population. Reduction of gastro-intestinal discomfort is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and reduction of gastro-intestinal discomfort.

Decreasing potentially pathogenic gastro-intestinal microorganisms (ID 2972)

- The claimed effect proposed for further assessment relates to a decrease in potentially pathogenic gastro-intestinal microorganisms. The proposed target population is the general

population. Decreasing potentially pathogenic gastro-intestinal microorganisms might be a beneficial physiological effect.

- A cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and decreasing potentially pathogenic gastro-intestinal microorganisms.

Improved lactose digestion (ID 2972)

- The claimed effect proposed for further assessment relates to improved lactose digestion. Improved lactose digestion is a beneficial physiological effect for individuals with lactose maldigestion.
- A cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and improved lactose digestion.

Increasing IL-10 production (ID 2973)

- The claimed effect proposed for further assessment relates to increasing IL-10 production. The proposed target population is the general population. The evidence provided did not establish that increasing IL-10 production is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of a combination of *L. paracasei* CNCM I-1688 and *L. salivarius* CNCM I-1794 and a beneficial physiological effect related to an increase in IL-10 production.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 for further assessment (No: EFSA-Q-2012-00200 and EFSA-Q-2012-00201). The scientific substantiation is based on the information provided by the competent Authority of Italy for further assessment of this claim (available on: <http://www.efsa.europa.eu/en/topics/topic/article13.htm>).

REFERENCES

- AAT (Advanced Analytical Technologies), 2011a, unpublished. Report on confirmation of the taxonomic identity of the bacterial strain, *Lactobacillus paracasei* I1688, using molecular methods.
- AAT (Advanced Analytical Technologies), 2011b, unpublished. Report on confirmation of the taxonomic identity of the bacterial strain, *Lactobacillus salivarius* I1794, using molecular methods.
- Bonetti A, Morelli L and Campominosi E, 2002. Assessment of the persistence in the human intestinal tract of two probiotic lactobacilli *Lactobacillus salivarius* I 1794 and *Lactobacillus paracasei* I 1688. *Microbial Ecology in Health and Disease*, 14, 229-233.
- Castellazzi AM, Valsecchi C, Montagna L, Malfa P, Ciprandi G, Avanzini MA and Marseglia GL, 2007. In vitro activation of mononuclear cells by two probiotics: *Lactobacillus paracasei* I 1688, *Lactobacillus salivarius* I 1794, and their mixture (PSMIX). *Immunological Investigations*, 36, 413-421.
- Castellazzi AM, 2007a, unpublished. Final report on Florilac Trial. University of Pavia.
- Dondi G, 2004. Use of agents active against *Candida* in the treatment of disorders of the oral and intestinal mucosa. US2004/0043011A1, United States Patent and Trademark Office.

- Dondi G and Malfa P, 2007. Use of specific lactic bacteria for the preparation of immunomodulating compositions. WO2007/015132A2, Organization WIP.
- Dondi G, 2007. Use of agents active against *Candida* in the treatment of disorders of the oral and intestinal mucosa. EP1339419B1, European Patent Office.
- EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2009. Scientific Opinion on the substantiation of health claims related to non-characterised microorganisms pursuant to Article 13 of Regulation (EC) No 1924/2006 on request from the European Commission. EFSA Journal, 7(9):1247, 64 pp.
- Jensen MA, Webster JA and Straus N, 1993. Rapid identification of bacteria on the basis of polymerase chain reaction-amplified ribosomal DNA spacer polymorphisms. Applied and Environmental Microbiology, 59, 945.
- Morelli L, 1996, unpublished. Identification of two strains of *Lactobacillus* for a patent deposit. Università Cattolica del Sacro Cuore di Piacenza.
- Morelli L, 1997, unpublished. Microbiological analysis of 6 strains of *Lactobacillus* for a patent deposit. Università Cattolica del Sacro Cuore di Piacenza.
- Pedraglio G, 2004. Novel *Lactobacilli* strains useful in the treatment of disorders of the gastrointestinal system. EP0861905B1, European Patent Office.
- Valsecchi C, Marseglia A, Licari A, Montagna L, Leone M, Marseglia G and Castellazzi AM, 2008. PSMIX nuova miscela brevettata a base di *L. paracasei* I-1688 e *L. salivarius* I-1794: attività probiotiche e razionale di impiego clinico. Archives of Medical Therapy, 2, 9-14.
- Ventura M, Casas IA, Morelli L and Callegari ML, 2000. Rapid Amplified Ribosomal DNA Restriction Analysis (ARDRA) Identification of *Lactobacillus* spp. Isolated from Fecal and Vaginal Samples. Systematic and Applied Microbiology, 23, 504-509.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods⁵ (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined as "any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

- a) the role of a nutrient or other substance in growth, development and the functions of the body; or
- b) psychological and behavioural functions; or
- c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

- (i) based on generally accepted scientific evidence; and
- (ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13 (1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD⁶

Foods are commonly involved in many different functions⁷ of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

⁵ OJ L12, 18/01/2007

⁶ The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

⁷ The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

- (a) the claimed effect of the food is beneficial for human health,
- (b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),
- (c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,
- (d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.
- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.
- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.
- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.
- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.
- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.

APPENDIX C

Table 1. Health claims related to a combination of *Lactobacillus paracasei* CNCM I-1688 and *Lactobacillus salivarius* CNCM I-1794 including conditions of use, as proposed in the framework of further assessment.

ID	Food or Food constituent	Health Relationship	Proposed wording
2972	PSMIX®: mixture of <i>Lactobacillus paracasei</i> CNCM I 1688 and <i>Lactobacillus salivarius</i> CNCM I 1794.	Is a probiotic; Contributes to a healthy digestive system by supporting the gut flora through an increased number of positive lactobacillus in the intestine; useful to maintain a healthy intestinal flora by adhering to the mucosa; Improves intestinal barrier function by competing (steric encumbrance) against pathogens; Reduces gastro-intestinal discomfort; Necessary to maintain a healthy digestive system by production of specific enzymes (eg: betagalactosidase).	PSMIX® is a probiotic mixture that maintains the balance of healthy intestinal microflora and regulates intestinal functionality by replacing normal, natural microflora (especially after antibiotic/antimycotic treatment) which contributes to reducing gastro-intestinal discomfort which, for example, could be due to problems in lactose digestion.
Conditions of use Being 'Generally Recognized as Safe' (GRAS) by the Food and Drug Administration, this health claim is destined for the general population. The advised condition of use of this constituent is of at least 1x10 ⁹ ufc per day. Since this product's release on the market, there have not been any reported cases of undesirable side effects due to this nutrient, however, italian national law imposes the use of these precautions on the product label: Do not exceed the indicated dosage; Keep out of reach of children under three years of age; The intake of this supplement is not meant as a substitute to a balanced diet and healthy lifestyle. This product is presented in a soluble powder form. Dissolve the content of one sachet in water or warm milk, and drink immediately. Should be consumed, preferably, on an empty stomach.			
ID	Food or Food constituent	Health Relationship	Proposed wording
2973	PSMIX® : mixture of <i>Lactobacillus paracasei</i> CNCM I 1688 and <i>Lactobacillus salivarius</i> CNCM I 1794.	Supports your natural (immune) defence system by increasing the IL-10 production in peripheral blood mononuclear cells (PBMC); As recommended by PASSCLAIM, the functional capacity of the immune system has been assessed by: measuring specific cell functions ex vivo, measuring specific cell function in vivo e.g. production of cvtokines or	PSMIX® is a probiotic mixture that helps to support natural defences by modulating natural immunological responses, and helps to support the development of the immune system by regulating an immunological response in subjects with allergic reactions or by stimulating immunological response during viral infections.

		response to antigens, and determining the incidence and severity of infection; Necessary to maintain the natural defences/helps to maintain a balanced immune system (increasing the IL-10 production).	
	<p>Conditions of use</p> <p>Being 'Generally Recognized as Safe' (GRAS) by the Food and Drug Administration, this health claim is destined for the general population.</p> <p>The advised condition of use of this constituent is of at least 1x10⁹ ufc per day.</p> <p>Since this product's release on the market, there have not been any reported cases of undesirable side effects due to this nutrient, however, italian national law imposes the use of these precautions on the product label: Do not exceed the indicated dosage; Keep out of reach of children under three years of age; The intake of this supplement is not meant as a substitute to a balanced diet and healthy lifestyle.</p> <p>This product is presented in a soluble powder form. Dissolve the content of one sachet in water or warm milk, and drink immediately. Should be consumed, preferably, on an empty stomach.</p>		

GLOSSARY AND ABBREVIATIONS

ARDRA	Amplified rDNA restriction analysis
CNCM	Collection Nationale de Cultures de Microorganismes, France
DNA	Deoxyribonucleic acid
PCR	Polymerase chain reaction
PFGE	Pulsed field gel electrophoresis
RAPD	Randomly amplified polymorphic DNA
Rep-PCR	Repetitive extragenomic palindromic – PCR
RNA	Ribonucleic acid